1642

ATTORNEY'S DOCKET NO. C1039.70035US00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	ARTHUR M. KRIEG ET AL.
Serial No.:	09/669,187
Conf. No.:	2999
Filing Date:	September 25, 2000
For:	IMMUNOSTIMULATORY NUCLEIC ACIDS
Examiner:	David J. Blanchard
Art Unit:	1642

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

The undersigned hereby certifies that this document is being placed in the United States mail with first-class postage attached, addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the 25th day of March, 2004.

Maria A. Trevisan, Reg. No. 48,207

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

Sir:

Transmitted herewith are the following:

[X] Response to Restriction Requirement
[X] Check in the amount of $2010.00
[X] Return Receipt Postcard

If the enclosed papers are considered incomplete, the Mail Room and/or the Application Branch is respectfully requested to contact the undersigned at (617) 720-3500, Boston, Massachusetts.

A five month extension of time is respectfully requested and the appropriate fee is submitted herewith. If an additional fee is required, please charge it to the account of the undersigned, Deposit Account No. 23/2825. A duplicate of this sheet is enclosed.

Respectfully Submitted,
Arthur M. Krieg., et al., *Applicants*

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Attorney's Docket No.: C1039.70035US00
Date: March 25, 2004
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RESPONSE TO SECOND RESTRICTION REQUIREMENT

Sir:

In response to the Second Restriction Requirement (paper # 17) mailed from the United States Patent and Trademark Office on September 25, 2003, Applicants have elected the claims of Group I, drawn to a method of stimulating an immune response with a Py-rich immunostimulatory nucleic acid, classified in class 424, subclass 278.1. Accordingly, the election relates at least to claims 1, 16-36, 77, and 85-94 (in part) and claim 2-15 and 98.

Applicants further elect an X_1X_2 dinucleotide motif that is TG and an X_3X_4 dinucleotide motif that is GT.

It is Applicants' understanding that upon allowance of claim 1 (i.e., the linking claim), the restriction as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claim will be entitled to examination in the instant application.

Applicants make this election with traverse for the reasons set forth below.

The Examiner has vacated the first Restriction Requirement and substituted it with the present Restriction but has not provided reasons for doing so. In response to the first Restriction

Requirement, however, Applicants cancelled several claims that were drawn to non-elected inventions. These cancelled claims however were not considered in the present Restriction Requirement.

The Examiner also states that the claims are presented in improper format, presumably based on the 10,240-way restriction (i.e., 40 groups, 16 X_1X_2 elections, and 16 X_3X_4 elections) or the 89,600-way restriction (i.e., 10 groups, 16 X_1X_2 elections, 16 X_3X_4 elections, and 35 cancer elections). Applicants maintain that the claims are in proper format and that the Restriction is improper.

Search and examination:

The pending claims relate to the use of pyrimidine (Py) rich or TG nucleic acids to stimulate an immune response (claim 1). Claims 2-75, 85-94 and 98 are all dependent from claim 1. Accordingly, each of these latter claims comprises administering a Py rich or TG nucleic acid to a subject to induce an immune response.

The Examiner states that the methods of Groups I-XL differ in the "method objectives, method steps and parameters and in the reagents used". Accordingly, the Examiner has restricted these dependents with respect to administration of other therapeutic agents such as peptide antigens (e.g., Groups III and IV), antibodies (e.g., Groups XXI and XXII; and Groups XXIX and XXX; and Groups XXXIII and XXXIV), chemotherapeutic agents (e.g., Group XXIII and XXIV), immunotherapeutic agents (e.g., Group XXV and XXVI), cancer vaccines (e.g., Groups XXVII and XXVIII), viral antigens (e.g., Groups XXXIII and XXXIV), bacterial antigens (e.g., Groups XXXV and XXXVI), parasitic antigens (e.g., Groups XXXVII and XXXVIII) or fungal antigens (e.g., Groups XXXIX and XL); and subject types such as subjects having or at risk of developing asthma (e.g., Groups XV and XVI), allergy (e.g., Groups XVII and XVIII), cancer (e.g., Groups XIX and XX), or infectious disease (e.g., Groups XXXI and XXXII).

The Examiner loses sight of the common underlying element of the pending claims (i.e., the use of a Py rich or TG nucleic acid to stimulate an immune response). Thus although the Examiner believes that examination of these Groups would require different searches in the

patent and literature databases, Applicants maintain that search and examination of claim 1 is co-extensive with search of claims dependent thereon. "If search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions." (MPEP 803.01). Search and examination of claim 1 and claims dependent thereon can be made without additional burden for the afore-mentioned reasons.

Nucleic acids:

The Examiner requires restriction of each of the X_1X_2 and X_3X_4 dinucleotide motifs to one of 16 possible dinucleotides for a total of at least 256 possible nucleotide sequences. The Examiner states that inventions A-P (relating to the various X_1X_2 and X_3X_4 dinucleotides) are unrelated "if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects". Furthermore the Examiner states that "where structural identity is required, such as for hybridization, the different sequences have different effects".

Applicants respectfully traverse. First, the nucleic acids of the pending claims are capable of use together. There is no teaching in the instant specification precluding such use. Second, the Examiner's contention that the nucleic acids have different modes of operation, different functions or different effects is unsupported. The members of each nucleic acid class share a common structural motif (e.g., a Py rich motif or a TG motif) and they mediate biological effects (e.g., immunostimulation) through the same mechanism. Third, the structural identity required in the invention (e.g., the nucleic acids must be Py rich or TG nucleic acids) is shared by the members of each nucleic acid class regardless of the nature of the flanking 5' or 3' dinucleotides, and is considered to be the essential factor contributing to the functionality of these nucleic acids.

The majority of dinucleotide motifs are present in claims reciting Markush groups (claims 8, 9, 71 and 72). The MPEP states that "it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention". (MPEP 803.02) Unity of invention exists in a Markush group that recites

compounds that (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility". (MPEP 803.02) The dinucleotide Markush group members satisfy both prongs of this test: they share the common utility of immunostimulation and they share the substantial structural feature of a poly T motif or a TG motif that is essential to immunostimulation. Accordingly, the nucleic acids embraced by the Markush groups in claims 8, 9, 71 and 72 should be examined together.

Nucleic acids that encode different proteins are considered unrelated by the Office. (MPEP 803.04) However, notwithstanding this assertion, the Commissioner has waived the requirements of 37 CFR 1.141 et seq. and permitted the claiming of a reasonable number of nucleic acid sequences in a single application, even though such nucleic acids could be completely structurally disparate. Moreover, the Office does not consider nucleotide sequences encoding the same protein to be independent and distinct, and continues to examine such sequences together, presumably without regard to the structural identity of such sequences. The MPEP states that exceptional cases in which less than 10 nucleotide sequences would be examined exist when the claimed material is of a complex nature (e.g., protein amino acid sequence reciting three dimensional folds).

The nucleic acids of the invention do not encode proteins. Rather, they are compounds that exhibit their functional effects without need for transcription or translation. Importantly, they may share more structural and functional identity than the *reasonable number of nucleic acid sequences encoding different proteins*, which the Office is willing to examine in a single application. Applicants further maintain that the nucleic acids of the pending claims are not of a complex nature, particularly since they are structurally defined by their primary nucleotide sequence alone, unlike protein amino acid sequences reciting three dimensional folds.

Cancers:

The Examiner states that inventions AA-BI (relating to 35 cancers) are unrelated "if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects." The Examiner states that these inventions represent characteristically different cancers which have different effects.

Applicants respectfully traverse. First, the invention relates to the use of Py rich or TG nucleic acids to stimulate immune responses and it is the effects of these nucleic acids with which the invention is concerned, not the "effects" of the 35 cancers. Second, the nucleic acids can be used in subjects having or at risk of having a cancer and, although it is common for a subject to have or be at risk for one cancer type, it is not impossible that a subject may have or be at risk for more than one cancer type (i.e., these cancer types are not necessarily mutually exclusive of each other). Third, whether the cancers have "different modes of operation, different functions, or different effects" is irrelevant given the nature of the invention (i.e., that nucleic acids of the invention can induce immune responses useful in the prevention or treatment of one or more of these cancers).

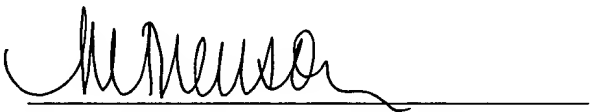
The Examiner concludes that the inventions are also distinct because they have acquired a separate status in the art due to their recognized divergent subject matter. The Examiner provides no support for this statement.

For at least these reasons, Applicants traverse and request reconsideration of the Restriction.

In telephone interviews with the Examiner on March 9th and 11th, Applicants proposed regrouping of Groups I, III, XV, XVII, XIX, XXI, XXII, XXV, XXVII, XXIX, XXXI, XXXIII, XXXV, XXXVII and XXXIX. These latter Groups commonly recite administration of Py-rich nucleic acids in a subject for the purpose of immunostimulation, and therefore Applicants believe their restriction is improper for at least the reasons stated above. The Examiner stated that he would consider such regrouping upon filing of this response. Applicants herein respectfully request such consideration from the Examiner. It is to be understood that Applicants do not intend by such request to forego the opportunity to link all pending claims at a later stage in prosecution, should the linking claim be found allowable.

Applicants expressly reserve the right to file one or more divisional applications on the subject matter of the non-elected claims. If the Examiner has any questions or comments, he is encouraged to contact the Applicants' representative at the number listed below.

Respectfully submitted,
Arthur M. Krieg, et al., *Applicants*



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